

## LUBRICIOUS COMPOSITION

### BACKGROUND OF THE INVENTION

The present invention relates to the field of lubricious compositions  
5 useful as coatings on surfaces of medical devices.

Improving the surface lubricity of insertable medical devices such as by  
application of lubricious polymeric coatings to the surfaces of such devices for the  
purpose of reducing friction between the surface of the medical device and other  
surfaces to which it comes into contact, such as when the device is introduced into the  
10 human body, is known in the art.

Catheters used for the delivery of other medical devices such as stents,  
stent-grafts, grafts, vena cava filters, dilatation balloons, as well as other expandable  
medical devices, and other medical devices used for introduction in blood vessels,  
urethra, body conduits and the like, and guide wires used with such devices are  
15 examples of articles which may be provided with lubricious coatings.

Guide catheters, and catheters for balloon angioplasty and biopsy are  
specific examples of such catheters.

Lubricious coatings of both a hydrophobic and a hydrophilic nature are  
known. Silicone is an example of a known hydrophobic lubricant.

20 Hydrogel polymers are also known lubricants and may be characterized  
by an initial non-tacky to tacky quality followed by lubricity upon hydration.

### SUMMARY OF THE INVENTION

The present invention relates to lubricious compositions useful for  
25 coating medical devices including at least one polymerizable component which is an  
alkoxylated acrylic based compound having at least two acrylate groups, and suitably  
three or more acrylate groups per molecule. The present invention also contemplates the  
use of the methacrylates as well.

As used herein, the term "compound" shall refer to monomers, oligomers  
30 and polymers.

The amount of alkoxylation is suitably about 1 to about 20 moles  
alkoxylate, more suitably about 2 to about 18 moles of alkoxylate, and more suitably  
about 3 to about 15 moles alkoxylate. Examples of alkoxylates include propoxylates  
and ethoxylates, as well as mixtures thereof.

Desirably, the alkoxyated (meth)acrylate compounds are non-aromatic alkoxyated (meth)acrylate compounds.

Suitably, the alkoxyated (meth)acrylate compounds have some water solubility of greater than about 15 wt-% and desirably even greater than about 50 wt-%.

5 In one embodiment, at least one alkoxyated trimethylol propane tri(meth)acrylate compound is employed in combination with at least one second component which provides lubricity.

One example of an alkoxyated trimethylol propane tri(meth)acrylate useful herein is ethoxyated trimethylol propane tri(meth)acrylate compound.

10 The second component may be any lubricious polymeric material, including lubricious hydrophobic lubricious polymers and hydrophilic lubricious polymers, as well as the hydrogels, or mixtures thereof. Crosslinkable materials may also be employed. Suitable polymers are disclosed in commonly assigned U.S. Patent No. 5693034 which is incorporated by reference herein in its entirety.

15 In one aspect of the invention, the crosslinker is employed with a noncrosslinked lubricious hydrogel polymer.

The polymerizable (meth)acrylate compound may also be employed with highly water absorbent polyurethanes such as those disclosed in commonly assigned copending U.S. Patent Application Serial no. 10/658718 which is incorporated by  
20 reference herein in its entirety. Such polyurethanes, typically aliphatic polyether polyurethanes, may be highly water absorbent, being capable of absorbing anywhere from about 500% to about 2000% water by weight. These polymers may be advantageously blended with polyurethanes having lesser water absorbency.

In another aspect, the polymerizable component may be employed in  
25 combination with at least one second polymerizable component. Examples of these types of compositions may be found in commonly assigned copending U.S. Patent Application Serial No. 10/658729 which is incorporated by reference herein in its entirety.

The above types of compositions often form what is referred to in the art  
30 as "semi-interpenetrating polymer networks" or "interpenetrating polymer networks".

A photoinitiator may be advantageously incorporated in the compositions of the present invention to facilitate crosslinking of the alkoxyated (meth)acrylate compound. Any suitable initiator used in combination with (meth)acrylates may be employed herein. Free radical type photoinitiators including, but not limited to,

benzophenones, ketones, acrylated amine synergists,  $\alpha$ -amino ketones, benzil ketals, find utility herein.

In one embodiment, at least one amino substituted ketone is employed. Examples of suitable  $\alpha$ -amino ketones include, for example, 2-methyl 1-[4-methylthio) phenyl] 2-morpholinopropan-1-one, 2-benzyl-2-(dimethylamine)-1-[4-morpholinyl)phenyl]-1-butanone.

Other optional additives may also be employed including, but not limited to, fillers, flow or viscosity modifiers, coupling agents, adhesion promoters, antioxidants, and so forth. Such additives are known to those of ordinary skill in the art. Of course, mixtures of any of the above materials may be employed in the composition as well.

The lubricious composition may be applied on the surface of medical devices or components thereof including polymeric and metallic surfaces to provide lubricity to such surfaces. The lubricious coatings find particular utility on medical devices and components thereof such as catheter shafts, guidewires, guidewire lumens, dilatation balloons, stent retaining sleeves, and so forth. Inner and outer surfaces and combinations thereof may be coated. The lubricious coatings may be employed on both inner and outer surfaces of such medical devices and components thereof.

In one embodiment, the medical device is a catheter device such as a guide catheter or a delivery catheter.

However, the lubricious coatings according to the present invention find utility for reducing frictional forces of any medical devices insertable in the body of a patient where one surface is movably in contact with another surface.

The surface of the device to which the lubricious composition of the present invention is to be applied may also first be primed or otherwise treated to improve the adhesion of the lubricious composition to the surface of the device. Such primers or treatments are known to those of skill in the art and include, amount others, coupling agents, primer compositions and plasma or corona treatments, for example.

The present invention further relates to a process for applying the lubricious coatings to the medical devices or components thereof. Such method includes the steps of applying the coating to the device or component thereof, and polymerizing the polymerizable material(s) on the surface of the device by administering UV radiation to the coated surface of the device. Application of the coating may be accomplished out

of solvent by spraying, brushing, painting, or so forth. Useful solvents include, but are not limited to, water, lower alcohols such as isopropanol, methanol and so forth.

Extrusion, coextrusion, and other application techniques may also be employed depending on the properties of the lubricant which is being used. Such techniques do not require the use of solvents.

Other benefits and advantages and will become apparent from the following description.

All patents discussed herein are incorporated by reference herein in their entirety.

## DETAILED DESCRIPTIONS OF THE INVENTION

While this invention may be embodied in many different forms, there are described in detail herein specific embodiments of the invention. This description is an exemplification of the principles of the invention and is not intended to limit the invention to the particular embodiments illustrated.

The present invention relates to a lubricious composition which may be employed on the surfaces of medical devices for reducing the friction between the lubricated surface, and at least one second surface.

The lubricious composition according to the invention includes at least one alkoxyated (meth)acrylate having at least two acrylate or methacrylate groups, and suitably three or more (meth)acrylate groups. The amount of alkoxylation is suitably from about 1 to about 20 moles, more suitably about 2 to about 20 moles, and even more suitably about 3 to about 20. It is more desirable having about 2 to about 18 moles of alkoxylation and most desirable having about 3 to about 15 moles of alkoxylation.

Examples of suitable alkoxyate groups include both propoxylates and ethoxylates as well as mixtures thereof.

Examples of suitable bi-, tri-, tetra-, etc. polyfunctional alkoxyated or polyalkoxyated acrylates include alkoxyated, desirably ethoxylated or propoxylated, neopentyl glycol diacrylates, butanediol diacrylates, trimethylolpropane tri-acrylates glyceryl triacrylates; and so forth.

In one embodiment, an alkoxyated trimethylol propane triacrylate monomer is employed, suitably an ethoxylated trimethylol propane triacrylate. Such compounds are available from Sartomer Company, Inc. in Exton, PA. Examples include SR454 having 3 moles of ethoxylation, a molecular weight of 454 g/mole and a water

solubility of 15 wt-% in water; SR499 having 6 moles of ethoxylation and a molecular weight of 560 g/mole; SR502 having 9 moles of ethoxylation and a molecular weight of 693 g/mole and SR9035 having 15 moles of ethoxylation and a molecular weight of 956 g/mole. Such compounds may also be found from Aldrich Chemical Co., Inc. in

5 Milwaukee, WI having from 1 mole of alkoxylation and greater.

Other examples of suitable alkoxyated (meth)acrylate compounds include, but are not limited to, propoxylated trimethylol propane tri(meth)acrylate, ethoxylated pentaerythritol tetra(meth)acrylate, propoxylated neopentyl glycol diacrylate, propoxylated glyceryl tri(meth)acrylate, trimethylolpropane ethoxylate (1  
10 EO/OH) methyl ether diacrylate, and so forth.

Suitably, the alkoxyated (meth)acrylate compounds have some water solubility of about 15 wt-% or more, and even more desirably, about 50 wt-% or more.

The aromatic alkoxyated (meth)acrylates tend to have little or no water solubility. For example, ethoxylated bisphenol A di(meth)acrylate, is classified as alkali  
15 soluble. However, this is not to say that some of the aromatic acrylates do not have water solubility and thus, if so, they may also be employed herein.

These acrylate compounds may be employed in amounts of about 0.1 wt-% to about 5 wt-%, and even more typically about 0.1 wt-% to about 2 wt-% based on a solvent or cosolvent blend.

20 The polymerizable materials are typically cured through the addition of actinic radiation such as ultraviolet (UV) radiation, e-beam radiation, or laser beam radiation may also be employed. The ethoxylated (meth)acrylate compounds, for the most part, cure via a free radical mechanism. They also may be sensitive to oxygen and can form stable radicals in its presence. Thus, it may be advantageous to employ an  
25 inert gas purge.

Crosslinking may be facilitated by the addition of a small amount of a photoinitiator. Any photoinitiator which is suitable for use in free radical curing mechanisms may be employed herein. Examples of suitable photoinitiators include, but are not limited to, benzophenones, acrylated amine synergists, ketone type, i.e. aromatic-  
30 aliphatic ketone derivatives, including benzoin and its derivatives, benzil ketals,  $\alpha$ -amino ketones, and so forth.

More specific examples of photoinitiators suitable for use herein include, but are not limited to, 2-phenyl-1-indanone; IRGACURE® 184 from Ciba Specialty

Chemicals, BENACURE® 184 from Mayzo and SARCURE® SR1122 from Sartomer, all of which are 1-hydroxyl cyclohexylphenyl ketone (HCPK); BENACURE® BP benzophenone; BENACURE® 651 and IRGACURE® 651, both of which are benzil dimethyl ketal or 2,2' dimethoxy-2-phenylacetophenone; BENACURE® 1173 2-  
5 hydroxy-2-methyl-1-phenyl-1-propanone; IRGACURE® 907 2-methyl 1-[4-methylthio) phenyl] 2-morpholinopropan-1-one; IRGACURE® 369 morpholinoketone; and so forth and blends thereof.

Photoinitiators are also available commercially in a variety of blends. Examples of commercially available blends include, but are not limited to, SARCURE®  
10 SR1136 is a blend of 4-methylbenzophenone and benzophenone; SARCURE® SR1137 is a blend of trimethylbenzophenone and methylbenzophenone; BENACURE® 500, a blend of 1-hydroxyl cyclohexylphenyl ketone and benzophenone;

The above lists are intended for illustrative purposes only, and not as a limitation on the scope of the present invention. One of ordinary skill in the art has  
15 knowledge of such photoinitiators.

Particularly suitable for use in combination with the (meth)acrylate type compounds of the present invention include the ketone type photoinitiators and the  $\alpha$ -amino ketones.

In one embodiment, at least one  $\alpha$ -amino ketone photoinitiator is  
20 employed. Examples of suitable  $\alpha$ -amino ketone photoinitiators include, but are not limited to, 2-methyl 1-[4-methylthio) phenyl] 2-morpholinopropan-1-one, 2-benzyl-2-(dimethylamine)-1-[4-morpholinyl)phenyl]-1-butanone or a mixture thereof.

It has been found by the present inventors, that the  $\alpha$ -amino ketone photoinitiators may be employed advantageously with any ethylenically unsaturated  
25 monomer and second lubricity providing component to arrive at an improved photocurable interpenetrating network. See for example, commonly assigned copending U.S. Patent Application Serial No. 10/658729, the entire content of which is incorporated by reference herein in its entirety.

Mixtures of any of the above photoinitiators may also be employed.  
30 Photoinitiators or blends thereof are typically used in amounts of about 0.01 wt-% to about 5 wt-%.

In another aspect, the present invention relates to the use of  $\alpha$ -amino ketone photoinitiators in combination with a polymerizable ethylenically unsaturated resin and at least one second component which provides lubricity.

Other optional additives may be employed in combination with the present invention including, but not limited to, flow or viscosity modifiers, antioxidants, coupling agents, and so forth.

Any suitable component which provides sufficient lubricity and is acceptable for use on medical devices implantable or insertable in the human body, may find utility herein. Suitably, such lubricating materials are biocompatible materials.

Both hydrophilic and hydrophobic polymeric materials find utility herein, as well as the special subclass of lubricious materials referred to as the hydrogels, and combinations thereof. However, hydrophilic polymers are most desirable.

Suitable examples of hydrophilic lubricants, include, but are not limited to, polyalkylene glycols and alkoxy polyalkylene glycols; copolymers of methylvinyl ether and maleic acid; maleic anhydride polymers; polyalkylene oxides, particularly the polyethylene oxides; poly((meth)acrylic acids); polymers of hydroxyl-substituted lower alkyl (meth)acrylates, such 2-hydroxyalkyl (meth)acrylate; polyvinylalcohols, hydrophilic polyamides; poly(meth)acrylamides; poly(N-isopoly(meth)acrylamides); poly(sodium-4-styrenesulfonates) and poly (sodium vinylsulfonates); poly(3-hydroxybutyric acids); poly(N-vinyl lactams) such as the polyvinylpyrrolidones; hydrophilic polyurethanes; polyethyleneimines; poly(sodium (meth)acrylates); methyl cellulose, hydroxymethyl cellulose, hydroxyethyl cellulose; polyvinylsulfonic acid; heparin; dextran and dextran sulfate and other modified dextrans; poly(saccharides); chondroitin sulphate; lecithin; and so forth, as well as copolymers thereof, and mixtures thereof. As used herein for purposes of simplicity, the term "copolymer" shall be used to refer to any polymer formed from more than one compound including the copolymers, terpolymers and so forth. Hydrophilic lubricants are described in commonly assigned U.S. Patent Application No. 6,458,867 which is incorporated by reference herein in its entirety.

Hydrophilic compounds are discussed in U.S. Patent No. 6503958 which is incorporated by reference herein in its entirety.

Hydrophilic polyurethanes, typically aliphatic polyether polyurethanes, which have high water absorbency being capable of absorbing anywhere from about

500% to about 2000% water by weight, may be employed herein. These types of polyurethanes are described in commonly assigned copending U.S. Patent Application Serial no. 10/658718 which is incorporated by reference herein in its entirety. These polymers may be advantageously blended with polyurethanes having lesser water  
5 absorbency.

Hydrogel polymers find utility herein. The above list of hydrophilic lubricants include some of which may be classified as "hydrogels". Hydrogels are known to absorb water and become slippery upon exposure to an aqueous environment. Examples of the hydrogels include, but are not limited to, polyethylene oxide,  
10 polyacrylic acid, polyacrylamides, poly(sodium 4-styrenesulfonates), poly(3-hydroxybutyric acids), polyvinylpyrrolidones, 2-hydroxyethyl methacrylates, and so forth. Hydrogels are known to those of ordinary skill in the art. Hydrogels are discussed in commonly assigned U.S. Patent No. 5693034 which is incorporated by reference herein in its entirety.

15 Molecular weights may range anywhere from 1,000 g/mole to 1,000,000 g/mole or more. Suitably, the weight average molecular weight of such polymers is from about 75,000 g/mole to about 1,000,000 g/mole and more suitably about 100,000 g/mole to about 750,000 g/mole. See for example, US 6262115 which discusses molecular weights of such hydrogels, the entire content of which is incorporated by  
20 reference herein in its entirety.

The above lists are intended for illustrative purposes only and not as a limitation on the present invention. One of ordinary skill in the art has knowledge of such hydrophilic polymeric materials.

Hydrophobic materials may be employed herein, although hydrophilic  
25 compounds are more desirable for use. Hydrophobic lubricants include, but are not limited to, silicones (i.e. organosiloxane polymers), functionalized silicones, hydrolyzable silanes which form silicones, fluorosilanes and other fluoropolymers, cellulose esters and ethers, ethyl cellulose, cellulose nitrate, cellulose acetate, cellulose acetate butyrate, cellulose acetate propionate, hydrophobic polyurethanes, polyacrylates,  
30 natural and synthetic elastomers, polyacetals, hydrophobic polyamides, polyvinylidene chloride, polycarbonate, homopolymers and copolymers of vinyl compounds, polyvinylchloride, glycerin, olive, vegetable, and other natural oils, and so forth. Some of these materials also form a gel-like substance, such as some silicones.



Molecular weights of the lubricants may range anywhere from 1,000 g/mole to 1,500,000 g/mole, desirably 50,000 to about 1,000,000 g/mole with those on the higher end being desirable.

Upon curing, the alkoxyated (meth)acrylate compounds may form what is referred to in the art as a “semi-interpenetrating network” or an “interpenetrating network” (IPN) with the lubricious material. Such networks may help to entrap the lubricious polymer on the surface to which it is applied.

Other optional ingredients may be incorporated into the compositions according to the invention including, but not limited to, flow or viscosity modifiers, antioxidants, coupling agents, surfactants, and so forth.

Examples of suitable flow modifiers include, but are not limited to, acrylic flow modifiers, fine silica powders, fine barium sulfate powders, fine particulate organic resins, clay-containing flow modifiers, polyamide-containing flow modifiers, urea-containing flow modifiers, urethane-containing flow modifiers, polycarboxylic acid salt-containing flow modifiers, cellulose-containing flow modifiers and so forth. Flow modifiers may be used in amounts of about 0.1 wt-% to about 5 wt-%, more suitably about 0.1 wt-% to about 1 wt-% and most suitably about 0.1 wt-% to about 0.2 wt-% based on a solvent or cosolvent blend of the composition.

Examples of suitable coupling agents include, but are not limited to, silanes, titanates, zirconates, and so forth. Coupling agents may be employed in amounts of about 0.01 wt-% to about 5 wt-%, more suitably about 0.01 wt-% to about 1 wt-%, and most suitably about 0.01 wt-% to about 0.1 wt-% based on a solvent or cosolvent blend of the composition.

The above lists are intended for illustrative purposes only and are not intended to limit the scope of the present invention. Other solvents not listed herein would find utility in the invention as well and are known to those of skill in the art.

In preparing the solution mixture of the present invention, the lubricity providing component and the ethylenically unsaturated resin or alkoxyated (meth)acrylate is admixed in a solvent or cosolvent mixture. Examples of suitable organic solvents of a more polar nature include, but are not limited to, the lower alcohols including, but not limited to, isopropyl alcohol and methanol; water; linear or cyclic carboxamides such as N,N-dimethylacetamide (DMAC), N,N-diethylacetamide, dimethylformamide (DMF), ethyl formamide, diethylformamide; N-methyl-2-pyrrolidone (NMP); dimethylsulphoxide (DMSO); acetonitrile; acetone and acetyl

acetone; acrylonitrile; benzonitriledimethyl acetamide; 1,4-dioxane; dipropyl sulfone; aromatic solvents such as toluene and xylene; nitrobenzene; phenylacetate; propionitrile; and so forth.

5 Other suitable organic solvents include, but are not limited to, aliphatic, cycloaliphatic or aromatic ether-oxides, more particularly dipropyl oxide, diisopropyl oxide, dibutyl oxide, methyltertobutylether, ethylene glycol dimethylether (glyme), diethylene glycol dimethylether (diglyme); phenyl oxide; dioxane, tetrahydrofuran (THF). Of course, any mixtures of the above-described solvents, i.e. cosolvent blends, may also be employed.

10 Examples of suitable solvents for use with hydrophobic lubricants include, but are not limited to, THF, chloroform, HFIP, DMF and so forth.

In the case of an alkoxyated (meth)acrylate monomer which 15 wt-% water solubility or more, water and lower alcohols may be satisfactorily employed as the solvent/cosolvent blend.

15 However, if an acrylate polymer is employed, it will be necessary to select a solvent based on the solubility of the acrylate polymer in the solvent/cosolvent blend. Such solvent selection is known to those of ordinary skill in the art.

If the lubricant is admixed in a solvent, the amount of lubricant is typically not more than about 5 wt-%, typically about 1 to about 5 wt-%. Of course, to  
20 some degree, this may depend on the viscosity of the polymer being employed.

The above list is intended for illustrative purposes only and not as a limitation on the scope of the present invention. One of ordinary skill in the art has knowledge of such solvents.

25 Surfactants may be advantageously employed to obtain a satisfactory mixture in the solvent or cosolvent blend. Any soluble surfactant or a mixture of surfactants in the above-mentioned solvents may be useful. Surfactants may be particularly advantageous where hydrophobic and hydrophilic materials, or other wise incompatible materials, are being admixed with one another.

The mixture may be applied to the medical device by any method known  
30 in the art including, but not limited to, spraying, dipping, painting, rolling, sponge painting, and so forth.

The coating will then be allowed to dry. The solvent may be more readily evaporated at an elevated temperature, although room temperature drying is acceptable. However, improved durability may be achieved by drying the coating at

elevated temperatures of, for example, 70°C. Suitably, drying is conducted at an elevated temperature over several hours to improve the durability of the coating. Crosslinkers which have a high enough molecular weight and which are not highly volatile, can be compounded directly with lubricant, allowing the use of extrusion or coextrusion techniques for applying the coating. Such techniques do not require the use of solvents.

Once a coating has been applied to a substrate, the coating may then be crosslinked by exposing the coating to heat or actinic radiation such as UV light for a short period of time. This can then trigger the polymerization and crosslinking of the ethylenically unsaturated resin or prepolymer. Suitably the mixture is cured using a high intensity ultraviolet lamp.

The crosslinked structure helps to retain the lubricant(s) on surfaces to which the coating is applied.

The lubricious coatings according to the invention find utility in the medical device industry, in particular for medical devices inserted in the body. For example, the lubricious coatings find utility on catheter devices, in particular, on guide wires, catheter shafts, dilatation balloons, stent retaining sleeves and so forth.

Dilatation balloons may be coated on the body, cone and/or waist portions or any combination thereof. In some embodiments, the balloon is coated on the distal and proximal waist cones, and on a portion of the body, but not in the center of the body. This has been found to reduce “watermelon seeding”, a term of art used to refer to slippage of the balloon during inflation in a lesion. This can be an issue in particular when the lesion is tapered, but this is not the only situation where “watermelon seeding” can occur.

The lubricity of the coating may be controlled through the use of different lubricants, as well as by the amount of lubricant added to the mixture. This can also allow for the use of different coatings on the same medical device such as different coatings on different portions of a catheter device where higher or lower lubricity may be desirable. For example, it may be desirable to coat the proximal portion of the catheter device with a less lubricious formula for better gripping, and to coat the distal portion of the device with a more highly lubricious coating for better trackability. This may be advantageous for guide wires or PV catheter assemblies.

The coating according to the present specification may be employed for drug delivery. A drug can be incorporated into the polymer network formed by the

crosslinked material which helps to entrap a drug(s) which can then more slowly leach out of the crosslinked network when the medical device is employed in the body.

The following non-limiting examples further illustrate the present invention.

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## EXAMPLES

### Example 1

5

Table 1

Isopropyl alcohol		Solvent	77.7 wt-%
Polyethylene oxide Mw = 1,000,000 g/mole		Lubricant	1.8 wt-%
Reverse osmosis water			19.765 wt-%
Ethoxylated trimethylol propane triacrylate	Sartomer SR-9035 (completely soluble)	crosslinker	0.2 wt-%
Acrylic	Modaflow AQ 3025	Flow modifier	0.1 wt-%
Silane		Coupling agent	0.025 wt-%
2-methyl 1-[4-methylthio) phenyl] 2-morpholinopropan-1-one	I-907	Photoinitiator	0.015 wt-%

The above disclosure is intended to be illustrative and not exhaustive.

This description will suggest many variations and alternatives to one of ordinary skill in this art. All these alternatives and variations are intended to be included within the scope of the claims where the term "comprising" means "including, but not limited to". Those familiar with the art may recognize other equivalents to the specific embodiments described herein which equivalents are also intended to be encompassed by the claims.

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